LTBI regimens and pre-treatment Counseling

Supporting Patients with LTBI Infection: What Nurses Need to Know
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Michelle Haas, M.D.
Associate Director
Denver Metro Tuberculosis Program
Denver Public Health

DISCLOSURES

• I have no disclosures or conflicts of interest to report
Objectives

• By the end of this presentation, participants should be able to:

  • Be able to discuss the rationale behind latent TB treatment with patients

  • Be able to discuss and recommend different LTBI regimens for patients

  • Be able to list side effects and when to stop/hold LTBI treatment

LTBI Treatment: Key considerations

Efficacy
• Ability to prevent disease among individuals adhering to medication

Effectiveness (adherence)
• Ability to prevent disease when used in public health practice

Drug interactions & adverse events

Monitoring requirements, cost, availability
Rifampin—our first line treatment for latent TB

- Rifampin (RIF) given daily for 4 months. Dosing for adults is 10mg/kg, max dose 600mg daily
  - Substantial drug interactions
  - Better completion rates compared to INH
- Obtain LFTs:
  - if aged >50
  - has underlying liver disease
  - pregnant/or within 3 months post-partum
  - Repeat only if abnormal or with symptoms
  - Regular EtOH consumption or taking other hepatotoxic agents

Isoniazid and Rifapentine both once weekly for 12 doses

- Isoniazid: 15 mg/kg, rounded up to the nearest 50 or 100 mg; 900 mg maximum
- Rifapentine
  - 10 to 14 kg: 300 mg
  - 14.1 to 25 kg: 450 mg
  - 25.1 to 32 kg: 600 mg
  - 32.1 to 49.9 kg: 750 mg
  - >50 kg: 900 mg maximum
- Obtain LFTs:
  - if aged >35
  - has underlying liver disease
  - pregnant/or within 3 months post-partum
  - Regular EtOH consumption or taking other hepatotoxic agents
Add B6 when patients take INH in the following scenarios

- Diabetes
- Chronic kidney disease
- EtOH abuse
- Malnutrition
- HIV infection
- Pregnant/post-partum
- Seizure disorders
- Consider offering to exclusively breastfed infants whose mother is on INH

Dose (adults)
- 25-50mg if given daily
- 100mg if given once per week

Isoniazid Regimens

Preferred
- INH daily for 9 months

Acceptable Alternatives
- INH twice/week for 9 months by DOT
- INH daily for 6 months
- INH twice/week for 6 months by DOT
Pregnancy, lactation, post-partum period

- Pregnancy does not increase TB risk
  - INH and Rifampin
    - Safe in pregnancy, no contraindication to breastfeeding
  - Trials of INH-rifapentine excluded pregnant women
- Higher hepatitis risk post-partum
- Indications for treatment of LTBI in pregnancy:
  - High risk contact
  - Immunocompromised

Children

Observational data: Denver Public Health 2006-15, change to 4R as 1st line LTBI Rx
- 4R: 84% - 330/395
- 9H: 69% - 536/779 p< 0.001
- Similar toxicity: 1.5, 0.8%

- UPDATE from Pediatric Red Book 2018
  - 3 months of INH-rifapentine if ≥ 2 years old (PK data pending for under 2)
  - 4 months rifampin and then INH in that order, all acceptable
  - INH x 9 mo. - Intermittent regimens used for DOPT

Gaensbauer J. PIDJ 2017.
Red Book: 2018-2021
TNF-α antagonists

- Treat if
  - TST ≥ 5mm  --- or ---
  - Positve IGRA  --- or ---
  - Epidemiologic risk (even if TST and IGRA are negative)—somewhat controversial
- Initiate TNF--α inhibitor after one month of LTBI treatment
  - Based on expert opinion

People Living with HIV: LTBI regimens

- INH daily for 9 months + B6 25mg daily
- Rifampin (RIF) given daily for 4 months
  - Substantial drug interactions, all medications should be reviewed
- INH-rifapentine once weekly for 12 doses
  - 2.6% HIV-infected—unclear if on ART in initial studies
  - Can now be given self-administered or as directly observed therapy
  - Likely safe if patients are on efavirenz or raltegravir based regimens

Podany, CROI abstract # 455, 2018
Weiner M, J antimicrob Chemother 2014
Laboratory Monitoring

Repeat laboratory monitoring if patient has:

- Abnormal baseline results
- Adverse effects
- High risk for adverse reactions
- Abdominal tenderness on exam
- Check CBC if flu-like illness or petechiae

Monthly Clinical Monitoring and follow-up

- Common side effects
  - Nausea
  - Burning epigastric pain
  - Rash
  - Fatigue
  - Dizziness
  - Headache

- Less common side effects
  - Vomiting
  - Flu-like illness
  - Jaundice
  - RUQ pain
  - Petechiae
  - Numbness/tingling in hands/feet (INH only)
Clinical Monitoring

- Stopping LTBI treatment
  - If LFTS are greater than 3X ULN and the patient has symptoms
  - If LFTS are greater than 5X ULN
  - When the patient is intolerant for other reasons

DPH 2006-2018: No. of LTBI Patients Starting INH, RIF, 3HP per Quarter

[Graph showing number of LTBI patients starting treatment from 2006 to 2018]
Patients starting & completing LTBI regimens: DMTB Clinic 2006-2018

<table>
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<tr>
<th>Regimen</th>
<th>Completed</th>
<th>Started*</th>
<th>% completed</th>
<th>% of Total</th>
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<td>3919</td>
<td>60</td>
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</tr>
<tr>
<td>4 RIF</td>
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<td>3916</td>
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<tr>
<td>3 HP</td>
<td>692</td>
<td>910</td>
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<tr>
<td>Total</td>
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<td>8745</td>
<td>67</td>
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</tbody>
</table>

*Excluding 347 starting other regimens over the 13 years.

Denver Metro TB Clinic: RN offering LTBI options

- “I generally review/offer all options assuming no medical contraindications.”
- “Patients do generally choose either 4R or 3HP, basically whether they can handle remembering a daily medication vs handle taking 10 pills at once – they usually have a strong preference one way or another!”
- “The only time I will not offer 3HP SAT is if I am worried that the patient doesn’t understand how to take the weekly regimen and may overdose.”
Tips from TB Clinic RN for INH-rifapentine:

**INH-rifapentine (anecdotal):**
- Ample hydration prior to 3HP dose and the day after.
- Transient nausea, dizziness immediately after dosing can be normal if it self resolves; *always* recommend dosing at night/after dinner for this reason.
- Taking with food helps with tolerability and adherence.

**Rifampin (anecdotal):**
- If preexisting GERD, daily rifampin may exacerbate that more than a once-weekly regimen. Taking with food greatly seems to greatly increase tolerability.
- Urine/body fluid discoloration is alarming, but normal, expected and *non-painful*.

**INH (anecdotal):**
- Reserved for young women who choose to rely solely on their hormonal BCM (the patient can make this decision!), moderate-significant drug interactions on rifampin (mainly with anticoags, ARVs, and psych meds), or previous rifamycin intolerance.

Patient concerns and questions:

Why should I take a medication for a bacteria that is dormant/sleeping?

Am I really infected with TB?

I feel fine, why do I need this medication?

I don’t want to risk lowering the effectiveness of my birth control

I am not sure this test is valid

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Suggested messaging

- It’s important to stay healthy. Even though the risk is low, having active TB can be life threatening. If you have active TB in your lungs this can be passed to other people. This puts your health and the health of your loved ones at risk.
- While the TB in your body is “sleeping” it is still an infection that could worsen. Treatment before you get sick will keep this from happening.
- No test is perfect. However, these are the best tests we have for TB infection. Most people who become infected with TB aren’t sure when or how it happened.
- We can find a regimen that will only minimally interact with your birth control.

Patient and parental concerns and questions

Are you sure that this is necessary?

I am worried about my child taking medication.

My son is very active and hates taking medication—how will I give this to him?

But he was never around anyone who was sick with TB.
Suggested messaging

It’s important for your son to stay healthy. Children are at very high risk for developing active TB and complications such as meningitis.

Most children do very well on treatment for latent TB and have no adverse effects.

Most of the time, we can’t pinpoint when we are infected with TB.

It’s always challenging to give children medication. We are here to support you. Many children are happy taking medication with food and/or cherry syrup.

Patient concerns and questions

I am worried about having side effects

Am I really infected with TB again?

I would like to get pregnant and may need to undergo IVF in order to get pregnant.
Suggested messaging

It’s reasonable to be concerned about adverse effects of treatment. If you do start treatment, we will do everything possible to support you and monitor you closely.

Most of the time, we can’t pinpoint when we are infected with TB. I don’t know for certain if you were infected again. But, there is a significant risk to you and your health.

I am here to support you and your plans to expand your family. This includes ensuring you stay as healthy as possible.

Summary

• Testing and treatment for TB infection (LTBI) should be prioritized for individuals who have lived in areas of ongoing TB transmission

• Identifying risk factors in a systematic way is challenging in clinical practice

• Public Health programs can strengthen TB Prevention efforts by partnering with providers in clinical practice
Questions?